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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/723,676	11/28/2000	Andrew A. Welcher	MBHB00-1214	6009

20306 7590 03/10/2003

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EXAMINER
MERTZ, PREMA MARIA

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/723,676	Welcher et al.
Examiner	**Art Unit**
Prema Mertz	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 16, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8, 10, 11, and 42-46* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 10, 11, and 42-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Amended claims 1-3, 10-11, 45-46 (Paper No. 12, 1/16/03) and original claims 4-8, 42-44 are under consideration.

2. Receipt of applicant's arguments and amendments filed in (Paper No. 12, 1/16/03) is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed in (Paper No. 12, 1/16/03):

(i) the objection to the title of the invention; and

(ii) the rejection of claims 1-2, 4-8, 10-11, 42-46, under 35 U.S.C. 112, first paragraph for compliance of the deposit requirements.

4. Applicant's arguments filed in Paper No. 12, 1/16/03, have been fully considered and were persuasive in part. The issues remaining are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101/112, first paragraph

6. Claims 1-8, 10-11, 42-46 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well established utility.

This rejection is maintained for reasons of record set forth at pages 3-6 of the previous Office action (Paper No. 10, 7/16/02).

Applicants argue that the specification teaches that the claimed nucleic acid encodes an amino acid sequence for IL-1ra-L polypeptide which shares a high degree of amino acid sequence identity with and IL-1β (31% identity) which are all members of the IL-1 family of proteins. However, contrary to Applicants assertions, it is clear from the instant specification that the instantly claimed nucleic acid molecule encodes what is termed an "orphan protein" in the art. There is only 31% identity between the protein encoded by the claimed nucleic acid and IL-1β. Hence there are only about 48 amino acids identical between the instantly instant protein and IL-1β and 107 different amino acids between the 2 proteins.

Applicant has traversed this rejection on the premise that members of the IL-1 family of proteins have been used as agonists or antagonists of inflammatory responses via binding to an interleukin receptor and therefore the claimed molecules have credible, specific and substantial utility. Applicants also argue that based on the expression of the human IL-1ra-L mRNA in adult T cells, liver, lung and spleen, placenta, fetal kidney, scalp and eye, the claimed molecules could be useful, for example, in agonizing an IL-1 receptor in T cells, liver, lung and spleen, placenta, fetal kidney, scalp and eye. However, the employment of a protein encoded by the nucleic acid of the instant invention, as an agonist is not a credible, substantial or specific utility. To grant Applicants a patent encompassing a nucleic acid encoding a isolated of as yet undetermined biological significance would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development,

without compensating benefit to the public" *Brenner v. Manson, Ibid*). To grant Applicant a patent on the claimed polynucleotide encoding a polypeptide based solely upon an assertion that the protein has 31% identity to IL-1β, 59% identity to L-1δ , and 44% identity to IL-1ϵ is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted.

The instant nucleic acid encodes a protein which has no demonstrated function. Applicants argue that the instant protein encoded by the claimed nucleic acid has substantial identity with IL-1η disclosed by Smith et al. (Exhibit B). However, contrary to Applicants arguments, there is 100% identity between IL-1η and the protein encoded by the claimed nucleic acid. Furthermore, the Smith et al. reference was published after the priority date of the instant invention and therefore has no bearing on the patentability of the nucleic acid of the instant invention. There has to be physiological significance for the polypeptide encoded by the nucleic acid disclosed in the specification. This requirement is analogous to basic scientific characterization, however, in the instant case no substantial benefit for the claimed protein is currently disclosed, but an exploratory significance. Furthermore, contrary to Applicants arguments, the employment of the polypeptides encoded by nucleic acids of the instant invention, as agonists of an IL-1 receptor is not a substantial or specific utility.

Applicants have failed to show in the instant specification, the practical benefit of the nucleic acid encoding the polypeptide of the instant invention. The Examiner is not questioning the fact that the instant protein is a member of the IL-1 family but that it has a specific function.

The Examiner's position is that this member of the family does not have a specific utility because different cytokines have different functions and the specific function of this particular protein has not been demonstrated in the instant application. The Examiner has presented a logical explanation that Applicants assertions are flawed. Applicants have failed to disclose what specifically the protein encoded by the claimed nucleic acid does. What is the physiological activity of the polypeptide of the instant invention?

Furthermore, the law requires that the invention be useful in currently available form. The Brenner case has been cited previously for the position that a substantial, specific utility of the polypeptide encoded by the claimed nucleic acid is required. There is no specific condition disclosed for which the product can be used. This requirement is analogous to basic scientific characterization, however, in the instant case no substantial benefit for the polypeptide is currently disclosed, but an exploratory significance. In the absence of a knowledge of the biological significance of the polypeptide, there is no immediately obvious "patentable" use for it. To employ the polypeptide of the instant invention as an agonist, is clearly to use it as the object of further research which has been determined by the Courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for the polypeptide encoded by the claimed nucleic acid, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

The following is an excerpt from M.P.E.P. 2138.05:

Utility for the invention must be known at the time of the reduction to practice. Wiesner v. Weigert , 212 USPQ 721, 726 (CCPA 1981) (except for plant and design inventions); Azar v. Burns , 188 USPQ 601, 604 (Bd. Pat. Inter. 1975) (a composition and a method cannot be actually reduced to practice unless the composition and the product produced by the method have a practical utility); Ciric v. Flanigen , 185 USPQ 103, 105 - 6 (CCPA 1975) ("when a count does not recite any particular utility, evidence establishing a substantial utility for any purpose is sufficient to prove a reduction to practice"; "the demonstrated similarity of ion exchange and adsorptive properties between the newly discovered zeolites and known crystalline zeolites ... have established utility for the zeolites of the count"); Engelhardt v. Judd , 151 USPQ 732, 735 (CCPA 1966) (When considering an actual reduction to practice as a bar to patentability for claims to compounds, it is sufficient to successfully demonstrate utility of the compounds in animals for somewhat different pharmaceutical purposes than those asserted in the specification for humans.); Rey - Bellet v. Engelhardt,181 USPQ 453, 455 (CCPA 1974) (Two categories of tests on laboratory animals have been considered adequate to show utility and reduction to practice: first, tests carried out to prove utility in humans where there is a satisfactory correlation between humans and animals, and second, tests carried out to prove utility for treating animals.).

A PROBABLE UTILITY MAY NOT BE SUFFICIENT TO ESTABLISH UTILITY

A probable utility does not establish a practical utility, which is established by actual testing or where the utility can be "foretold with certainty." Bindra v. Kelly , 206 USPQ 570, 575 (Bd. Pat. Inter. 1979) (Reduction to practice was not established for an intermediate useful in the preparation of a second intermediate with a known utility in the preparation of a pharmaceutical. The record established there was a high degree of probability of a successful preparation because one skilled in the art may have been motivated, in the sense of 35 U.S.C. 103, to prepare the second intermediate from the first inter mediate. However, a strong probability of utility is not sufficient to establish practical utility.); Wu v. Jucker , 167 USPQ 467, 472 (Bd. Pat. Inter. 1968) (screening test where there was an indication of possible utility is insufficient to establish practical utility). But see Nelson v. Bowler , 206 USPQ 881, 885 (CCPA 1980) (Relevant evidence is judged as a whole for its persuasiveness in linking observed properties to suggested uses. Reasonable correlation between the two is sufficient for an actual reduction to practice.)."

In conclusion, Applicants arguments with respect to utility of the polypeptide encoded by the instant nucleic acid, are found to be non-persuasive. Contrary to Applicants arguments, the instant specification does not disclose a single credible, specific or substantial utility for the instant polypeptide. The initial burden to demonstrate or present such is on Applicants.

Claims 1-8, 10-11, 42-46 also remain rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Claims 1-8, 10-11, 42-46 stand rejected under 35 U.S.C. § 112, first paragraph, because the instant specification does not teach how to use the invention for those reasons of record in pages 3-6 of the previous Office action (Paper No. 10, 7/16/02).

Claim Rejections - 35 USC § 112, first paragraph

7. Claims 2, 3-8, 10-11 and 42-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons of record set forth at pages 8-9 of the previous Office action (Paper No. 10, 7/16/02).

Applicants argue that claim 3 has been amended to recite "an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO:2

with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO:2...." and that the instant application teaches the amino acid sequence of human IL-1ra-L polypeptide shares a high degree of amino acid identity with two other members of the IL-1 family, 59% identity to L-1δ , and 44% identity to IL-1ϵ. However, contrary to Applicants arguments, the issue here is that Applicants are not in possession of the invention as claimed. Applicants appear to have misconstrued the Examiner's rejection. The issue here is that Applicants are claiming nucleic acid molecules encoding polypeptides, which nucleic acid molecules are not described in the specification. Furthermore, other than a nucleotide sequence encoding a polypeptide of SEQ ID NO:2, the specification does not disclose any other nucleic acid molecule with respect to the disclosure of relevant identifying characteristics i.e. structure, other physical and/or chemical characteristics or combination of such characteristics. In this case, in the instant specification, Applicants have failed to describe the modified nucleic acid with a single amino acid substitution. Furthermore, the claim recites "at least one modification" with no upper limit to the number of modifications. Thus, at the time the application was filed, the nucleic acids being claimed were not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention.

Furthermore, with respect to the 35 U.S.C. 112, first paragraph enablement rejection, Applicants appear to have also misconstrued this rejection. Applicants argue that claims 2-3 have been amended so that they no longer recite "variants". However, contrary to Applicants arguments, the

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issue here is that the "hybridizing" language and "at least 70 percent identical language" encompasses variants. Moreover, the specification is not enabled for a single nucleic acid encoding a polypeptide having an amino acid sequence anything less than the natural polypeptide.

The claimed invention encompasses modified nucleic acid molecules not envisioned or described in the specification, and neither does the specification disclose how the recombinantly produced nucleic acid molecules can be distinguished from each other. The specification does not provide the necessary information nor the guidance to enable a skilled artisan to make all the embodiments which would be encompassed by the scope of the claims since the claims do not recite the specific properties characteristic for the claimed nucleic acid encoding the polypeptide. The instant disclosure is clearly insufficient support under the first paragraph of 35 U.S.C. § 112.

Claim rejections-35 U.S.C. 112, second paragraph

8. Claims 1-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth at pages 12-14 of the previous Office action (Paper No. 10, 7/16/02).

Applicants argue that claims 1-3 have been amended to recite "hybridizes under at least moderately stringent conditions" which claims as amended are not indefinite. However, contrary to Applicants arguments the definition of moderately stringent conditions in the instant specification is "exemplary" and therefore the claims remain vague and indefinite.

Claims 4-8, 10-11, 42-46 are rejected as vague and indefinite insofar as they depend on claims 1-3 for their limitations.

Claim Rejections - 35 USC § 102

9. Claims 1-8, 10-11, 42-46, are rejected under 35 U.S.C. 102(a) as being anticipated by WO 9937662 (1999).

This rejection is maintained for reasons of record set forth at pages 14-15 of the previous Office action (Paper No. 10, 7/16/02).

Applicants argue that the instant specification teaches that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 17, lines 17-18) and that the cDNA molecule disclosed in the reference would not hybridize to the nucleotide sequence of SEQ ID NO:1 under these recited stringency conditions. However contrary to Applicants arguments, on page 17, lines 17-18, Applicants recite "by way of example" indicating that the moderately stringent conditions are exemplary. Therefore, the reference anticipates the claims.

10. Claims 1-8, 10-11, 42-46 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 855 404 A1 (1998).

This rejection is maintained for reasons of record set forth at pages 15-16 of the previous Office action (Paper No. 10, 7/16/02).

Applicants argue that the instant specification teaches that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of

approximately 79% (page 17, lines 17-18) and that the cDNA molecule disclosed in the reference would not hybridize to the nucleotide sequence of SEQ ID NO:1 under these recited stringency conditions. However contrary to Applicants arguments, on page 17, lines 17-18, Applicants recite "by way of example" indicating that the moderately stringent conditions are exemplary. Therefore, the reference anticipates the claims.

11. Claims 1-8, 10, 42 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,075,222 (1991).

Applicants argue that the instant specification teaches that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 17, lines 17-18) and that the cDNA molecule disclosed in the reference would not hybridize to the nucleotide sequence of SEQ ID NO:1 under these recited stringency conditions. However contrary to Applicants arguments, on page 17, lines 17-18, Applicants recite "by way of example" indicating that the moderately stringent conditions are exemplary. Therefore, the reference anticipates the claims.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 305-3014 or (703 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 746-5300.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
February 14, 2003